Intracranial Tumors Using Magnetic Resonance Spectroscopy

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The authors declare that they have no affiliations with or involvement in any organization or entity with any financial interest in the subject matter or materials discussed in this manuscript.

CONSENT
Yes, all information regarding the participants was guaranteed to remain private, as obtained from the college, with a consent form for all patients. No personally identifiable information regarding specific subjects was included in this study.

HUMAN AND ANIMAL RIGHTS
Ethical approval for this study was granted (ES-2022-0089) and with the Helsinki Declaration of 1975, as revised in 2000 (5).

ABSTRACT

Magnetic resonance spectroscopy (MRS), which can identify and measure brain components (metabolites) in pathological lesions and normal-appearing tissues, offers a valuable additional diagnostic tool for assessing several neurological diseases. The study aimed to determine how MRS helps distinguish chemical shifts in brain lesions. Materials and Methods: Three MRS cases were retrospectively evaluated among patients from the Saudi German Hospital between February and April 2023. Results: In MRS, a high choline/creatinine ratio with a drop in NAA was indicative of a high T2 flare and illness progression, confirming a space-occupying lesion (SOL) after left frontal craniotomy. MRS curve analysis showed a small area of the reversed choline/N-acetyl aspartate (NAA/choline) curve. There is a perifocal area of altered signal that could present gliosis rather than edema due to the absence of significant positive mass defects. The final impression was right parieto-occipital diffuse astrocytoma (G2). The last case, MRS, has a low choline-to-creatinine ratio and is likely to be inactive in Baló concentric sclerosis. Conclusions: MRS is a crucial technique for analysis and routine monitoring of brain malignancies. MRS may be useful and helpful in some situations and may aid in determining the extent of the disease or the location of hotspots.

CASE REPORT

BACKGROUND AND INTRODUCTION

Magnetic resonance spectroscopy (MRS) is a valuable tool for imaging brain tumors, primarily as an adjunct to conventional imaging and clinical presentation. Additionally, they can provide important information regarding cellular metabolism. Indeed, particular metabolites that vary in concentration depending on the clinical state of the tissue constitute tissues. They are typically used in biology and medicine. This method represents a distinctive noninvasive instrument for the real-time detection and quantification of anatomical cellular metabolic activities [1]. The primary distinction between magnetic resonance imaging (MRI) and MRS is that while MRS detects the chemical composition of the scanned tissue, it emits radiofrequency depending on the spatial position of the nuclei [2]. While MRS produces a graph or "spectrum" that displays the kinds and amounts of chemicals present in the brain or other organs, MRI produces an image and to measure MR spectra in vivo, one must be able to define the spatial origin of the detected signal.

Currently, 2 methods exist to obtain the spatially localized metabolic information in vivo: (a) single voxel spectroscopy (SVS) uses selective excitation pulses to localize a voxel of typically 3 to 8 cm^3 and (b) multivoxel arrays of spectra (MRS imaging) can be obtained in 1, 2, or 3 dimensions resulting in individual voxel sizes of typically 0.5to 3 cm^3 [2,3]. Important metabolites and ratios that affect clinical management include choline/creatine (Cho/Cr), choline/N-acetyl aspartate (Cho/NAA), lactate (Lac), Lac/Cr, Glucose (Glc), glutamine (Gln), CH2 Lipids (CH2-Lip), taurine (Tau), citrate (Cit), and alanine (Ala). The importance of analyzing the entire spectral profile

is emphasized using multidimensional analysis and artificial intelligence [4]. (MRS) of the human brain is an established methodology used clinically in many medical facilities worldwide for the evaluation of brain tumors. It was first published > 20 years ago. Although studies on human brain tumors have used heteronuclear elements such as phosphorus (31P) and sodium (11Na), most spectroscopic studies have used proton (1H) nuclei because of their high sensitivity and simplicity of use with commercial MRI scanners. Therefore, this review focuses on proton MRS in human brain tumors [5]. Brain tumors continue to be a leading cause of morbidity and mortality and are frequently resistant to treatment. The classification of brain tumors has a significant impact on clinical care [6]. Histopathological diagnosis, which requires sampling during an open or stereotactic neurosurgical operation, is the gold standard for tumor grading [7]. Metabolic imaging is a potentially useful diagnostic method for assessing brain tumors [8] and is currently being evaluated and graded using (MRS) as a key modality [7, 9]. Biopsies are frequently required to diagnose malignancies, because traditional MRI and other forms of biomedical imaging only allow hazy identification and localization of lesions. Unfortunately, many tumors are inaccessible to biopsy. The grading of tumors using MRS has also benefited from its noninvasive diagnostic method. MRS is a crucial tool for determining the type and grade of tumors as well as for determining the effectiveness of therapy [10]. Cutting-edge MRI methods such as MRS can aid in the resolution of challenging cases and boost diagnostic confidence. However, caution should be exercised when interpreting the results. These cutting-edge MR methods are helpful in both clinical and research settings; however, they should be viewed as supporting evidence for neurodiagnosis alongside the patient's clinical history, physical examination, and traditional MRI findings [10]. The main purpose of these cases is to provide knowledge on tumor biology and the clinical use of MR methods and to identify microvascular features, tumor type, grade, invasiveness, and degree of hypoxia. In these cases, we can represent the biochemical graph displayed by MRS, indicating whether the lesion under evaluation is benign or malignant, and determine the MRI values that are used as benchmarks to describe brain cancer.

INTRODUCTION

Currently, this examination can be completed within 15 minutes and can provide important clinical data that would enable a more accurate diagnosis. These include establishing an extended local assessment of morphological abnormalities observed on conventional MRI, better characterization of brain tumors, differentiating brain tumors from abscesses, and defining the tumoral characteristics of the investigated lesion. MRS is additionally employed by clinicians for treatment follow-up to determine the most active region of the lesion, plan and execute the biopsy, and distinguish between recurrent tumors and radionecrosis. This method can be used in radiosurgery to determine whether the radiation dose should be increased or decreased during tumor treatment. This retrospective study was conducted among patients from the Saudi German Hospital between February 2023 and April 2023. The study included three case 2 male and one female patient with ages range from–20-80 years came who underwent MRI and Spectroscopic analysis of the brain. The data will be collected using a data sheet with different variables (age, sex, pulse sequence used-protocol-scan plane-MRI finding, MRS report, etc.) Ethical considerations: Ethical approval for this study was granted (ES-2022-0089). All information regarding the participants was guaranteed to remain private, as obtained from the college, with a consent form for all patients. No personally identifiable information regarding specific subjects was included in this study.

The goal of this study was to develop a trustworthy, user-friendly, and effective system for the automatic, non-invasive classification of neoplasms in both academic and private practice radiology settings. It also aims to establish a universal database of perfusion and spectroscopic data that can be accessed and shared by the users. Sadly, this is not an easy task, made more challenging by the fact that even within the World Health Organization (WHO) classification of brain tumors, there are numerous subtypes of tumors, and there are times when even pathologists may disagree with the primary neuropathological diagnosis. Grade 1 cases of glioma (pilocytic astrocytoma), grade 2 (oligodendroglioma), grade 3 (anaplastic glioma, which includes anaplastic oligoastrocytoma and anaplastic oligodendroglioma), and grade 4 (glioblastoma multiforme) are classified by WHO. Grade I/II gliomas are classified as low-grade gliomas, according to clinical standards, whereas grade III/IV gliomas are classified as high-grade gliomas. Using a parametric approach, the mean Cho/NAA and Cho/Cr ratios were compared between the tumor grades. The metabolic ratios of high-grade gliomas and metastatic cases were also compared. The mean differences were considered statistically significant at a p value of 0.05. This is related to the samples, biopsy, inter-observer variability, and intra-observer variability, among other factors. Sampling errors can also occur when the ROI is placed in a perfusion analysis, and when voxels are placed in a 2D or 3D CSI matrix.118,119 We are also looking at ways to automate this volume of interest selection (INTERPRET). Furthermore, if perfusion and spectroscopy protocols, sequences, and methods are standardized, only a universally applicable system is possible. However, a summary of the developments in this pattern recognition method for noninvasive diagnosis of brain tumors is provided. These automated and semi-automatic methods have improved the capacity of classifying intracranial neoplasms using MRS sequences with various TEs, SVS, and CSI techniques. Overall, this method of computer-assisted diagnosis may improve, and doing so with perfusion and spectroscopic data may further increase our capacity to differentiate intracranial cancer. The percentage of correct classifications varied from 55 to 100%; however, overall, this method uses computer-assisted diagnosis. Molecules, such as protons and hydrogen ions, were examined using MRS. Proton spectroscopy was used more frequently. To distinguish between distinct tumor types, several metabolites

or byproducts of metabolism, including amino acids, lipids, lactate, alanine, N-acetyl aspartate, choline, creatine, and myoinositol, were analyzed. However, in our case study, we focused on only paying attention to four chemical shifts. These were CREATINE, CHOLINE and NAA. Additionally, the proportions of creatine, choline, and NAA were determined.

CASE 1

This report was authored by a consultant from the Radiology Department of a Saudi German hospital. 38 years was referred to the MRI department for brain magnetic resonance imaging (MRI) with contrast and spectroscopic analyses. The images show a space-occupying lesion in the sagittal frontal lobe measuring 17 × 14 × 16 mm in maximal dimension compared with 12 × 8 × 15 mm in the preceding examination, showing an increase in the size and signal of the left frontal lobe complex process, displaying high T2 and low FLAIR signals. Interval stability in size and signal of the previously seen diffuse abnormally high T2/FLAIR signal involving the bilateral medial temporal lobes, bilateral external capsule, posterior limb of the external capsule, brainstem, and periaqueduct region. In MRS, a high choline/creatinine ratio with a decrease in NAA level is indicative of high T2 flares and illness progression. This was likely a space-occupying lesion (SOL)after the left frontal craniotomy.

CASE 2

65 years old man come the MRI department complaining of persistent headache, blurred vision, and worsening seizures in the morning. Examination was done using 1.5 Tesla closed magnet MRI with contrast and spectroscopic analysis. MRI findings showed equivocal thinner enhancement in the right parietal residual apace occupying the lesion in relation to the surgical defect, with no diffusion restriction and a small area of reversed NAA/choline curve. There is a perifocal area of altered signal that could present with gliosis rather than edema due to the absence of significant positive mass defects. The final impression was a right parieto-occipital diffuse astrocytoma (G2).

CASE 3

31 years male with No Hypertension (HTN), No Diabetes mellitus (DM), glaucoma, or neck pain radtring to the chest wall came to the radiology department for MRI with CM and MRS analysis. The finding is a well-defined oval lesion with an abnormal signal located in the left posterior parietal region along the sptocollosal interface, it measures 1x1.5x1 cm, there is no surrounding mass effect or edema, and no diffusion restriction, which demonstrates low T1 signal, high T2 signal, and peripheral concentric ring of low and high signal seen in the FLAIR images. There was no evidence of postcontrast pathological enhancement. MRS has a low choline-to-creatinine ratio, which is likely to be inactive in Baló concentric sclerosis.

RESULTS

The noninvasive characterization of intracranial neoplasms can be significantly improved using MRS. However, the relatively low specificity and considerable subjectivity of interpretation continue to be significant obstacles in the implementation of these procedures. Recently, numerous researchers have attempted to create reliable automated systems for categorization of neoplasms. In Chart (1), we determined how brain lesions can be classified as MRS (Chart 1).

DISCUSSION

According to our study, MRS may assist in identifying the type and grade of a brain tumor by sensing its chemical changes, thus avoiding the need for intrusive treatment, as in case (2), the right parietal residual apace occupying the lesion seen in relation to the surgical defect, with no diffusion restriction and a small area of reversed NAA/choline curve. There is a perifocal area of altered signal that could present with gliosis rather than edema, due to the absence of significant positive mass defects. The final impression was Grade 2 right parieto-occipital diffuse astrocytoma, as in the study by Hellström et al. (2018), who found 70 non-neoplastic lesions, 43 low-grade tumors, and 95 high-grade tumors; in terms of MRI, the classification was correct in 130 cases (62%), uncertain in 39 cases (19%), and erroneous in 39 cases (19%). When MRS was included, 134 (64%) cases were accurate, 51 (25%) were incorrect, and 23 (11%) were uncertain. Additional MRS data were helpful or very helpful in 31 instances (15%) and misleading in 36 instances (17%) [12]. Our study included in case (1) a brain lesion with a maximum dimension of 17 × 14 × 16 mm, In MRS, a high choline/creatinine ratio with a drop in NAA is indicative of a high T2 flare and illness progression. This is likely space occupying lesion (SOL) after left frontal craniotomy, compare this case with similar brain lesion by Pyka et al. Of the 67 patients, nine (13.5%) had gliomas classified by the WHO as grade II, 14 (20.9%) as grade III, and 44 (65.7%) as glioblastomas. When we evaluated the study to check for similarity and correlation with our study, we found that all cases were correlated from the brain lesion side, and the instruments used were MRS, and they found in their study the differences between the grade of glioma, which was 13.5% and the median Overall survival (OS) was 12.4 months (range 0.7-78.8 months) [13, 14]. After evaluating The WHO study to check for similarity and correlation with our study, we found that all cases were correlated from the brain lesion side, and the WHO grade ||| glioma was 20% [14].

TEACHING POINT

We discovered that the major drawback of MRS is the dearth of cases due to insufficient research on the use of MRS metabolic ratios in the staging of brain tumors and not yet implemented MRS as a routine protocol.

CONCLUSION

MRS is a crucial technique for analysis and routine monitoring of brain malignancies. A biochemist with deeper knowledge of this technology would aid in its rapid and logical development, and a radiologist working closely with that scientist would permit the definitive use of the technology. Although the utility of MRS in the diagnosis and evaluation of the treatment

response of brain tumors has been widely documented, it has not been widely accepted as a routine clinical tool. MRS may be a useful addition to MRI and MRS, as routine brain MR examinations do not appear to be necessary; however, they can be helpful in some situations and may aid in determining the extent of the disease or the location of hotspots. We discovered that the major drawback of MRS is the dearth of cases due to insufficient research on the use of MRS metabolic ratios in the staging of brain tumors. We advise future studies to use a larger sample size because treatment is very expensive, unavailable in most clinics, not used as a routine examination, or not yet implemented in their protocols.

QUESTIONS

Question 1: Which of the following radiographic modalities provide information regarding cellular metabolism and metabolites?

1. Magnetic resonance angiogram.
2. Computed Tomography.
3. Magnetic resonance spectroscopy. (applies)
4.Conventional radiography.
5.Interventional Radiology.

Explanation:

1. Magnetic resonance angiogram. [Magnetic resonance angiography (MRA) is a group of techniques based on magnetic resonance imaging (MRI) to image blood vessels]

2. Computed Tomography. [is a type of imaging that uses X-ray techniques and computer to create cross-sectional images, also called slices, of the bones, blood vessels and soft tissues inside the body.]

3. Magnetic resonance spectroscopy. [they can provide important information regarding cellular metabolism. Indeed, particular metabolites that vary in concentration depending on the clinical state of the tissue constitute tissues.]

4. Conventional radiography. [Conventional Radiography. X-ray is an imaging technique that is used to show abnormalities in bones and bone density,]

5. Interventional Radiology. [Interventional radiologists use x-rays, ultrasound, CT, MRI, or other imaging guidance to navigate small instruments, like catheters and needles, through the body into blood vessels and/or organs to treat a variety of diseases..]

Question 2: Which of the following nuclei does not deal with MRS and MRI scanners?

1. phosphorus (31P).
2. sodium (11Na).
3. proton (1H).
4. Manganese 25. (applies)
5. carbon (^{13}C)

Explanation:

1. phosphorus (31P). [has become feasible and is of interest to obtain spatially and temporally resolved information that can be used for biomedical and diagnostic applications.]

2. sodium (23Na). [play important role in improving diagnosis, disease characterization, and clinical monitoring in neurologic disease.]

3. proton (1H). [nuclei of potential neurobiologic interest have a property known as magnetic moment and it had high sensitivity and ease of implementation on commercial MRI scanners.]

4. Manganese 25. (applies) [is one of ferromagnetic material which are strongly attracted to a static magnetic field and present the greatest danger to patients and staff in the MRI environment.]

5. carbon (^{13}C).[it is used as a functional medical imaging technique for probing perfusion and metabolism using injected substrates as Hyperpolarized carbon-13 MRI]

Question 3: Which of the following is not metabolites used to distinguish between distinct tumor types?

1. amino acid.
2. N-acetyl aspartate.
3. choline,.
4. uric acid. (applies)
5. creatine.

Explanation:

1. amino acid. [Amino acid metabolism plays an important role in tumor biology and tumor therapy. Accumulating evidence has shown that amino acids contribute to tumorigenesis and tumor immunity.]

2. N-acetyl aspartate. [it plays a critical role across various cell types and its significance in pathophysiological contexts, including Canavan disease and cancer metabolism.]

3. choline. [plays a cardinal role in several pivotal biological mechanisms, chiefly in safeguarding cell membrane integrity, orchestrating methylation reactions, and synthesizing vital neurotransmitters.]

4. uric acid. (applies) [Uric acid is a product of the metabolic breakdown of purine nucleotides, and it is a normal component of urine and not related to tumor type differentiation.]

5. creatine. [Creatine is a nitrogen-containing organic acid naturally existing in mammals. It can be converted into phosphocreatine to provide energy for muscle and nerve tissues. Creatine and its analog, cyclocreatine, have been considered cancer suppressive metabolites.]

Question 4: Which of the following is correct regarding single voxel spectroscopy (SVS)?

1. individual voxel sizes used.
2. typically 0.5to 3 cm^3.
3. multivoxel arrays of spectra.
4. one voxel 3 to 8 cm^3 (applies)
5. can be obtained in 1, 2, or 3 dimensions.

Explanation:

1. individual voxel sizes used. [This is multivoxel arrays spectrum which allows to use many voxels size.]

2. typically 0.5to 3 cm^3. [This is multivoxel arrays spectrum which allows to extend the voxel measurement to 0.5-3 cm^3.]

3. multivoxel arrays of spectra. [This is another type of spectrum used in MRS.]

4. one voxel 3 to 8 cm^3 (applies) [single voxel spectroscopy (SVS) is used one voxel and its measurement from 3-8 cm^3.]

5. can be obtained in 1, 2, or 3 dimensions. [This is multivoxel arrays spectrum which allows to use many dimensions.]

Question 5: Which of the following is not type of brain lesions?

1. astrocytoma.
2. Glioma.
3. A Mastocytoma. (applies)
4. Glioblastoma.
5. Baló concentric sclerosis.

Explanation:

1. astrocytoma. [Astrocytoma is a type of brain tumor. Astrocytomas (also astrocytomata) originate from a specific kind of star-shaped glial cell in the cerebrum called an astrocyte.]

2. Glioma.[A glioma is a type of primary tumor that starts in the glial cells of the brain or spinal cord.]

3. A Mastocytoma .[is a tumor of mast cells, which are derived from myeloid stem cells and located in connective tissues, predominantly in the skin and mucosal linings.]

4. Glioblastoma. [is a type of highly malignant brain tumor that starts and grows in the brain.]

5. Baló concentric sclerosis. [Baló concentric sclerosis (BCS) is a CNS inflammatory demyelinating disease characterized by alternating rings of demyelination and relatively preserved myelin, The lesions caused by Balo's disease look like bull's-eye marks, which is why it is also known as Balo's concentric sclerosis.]

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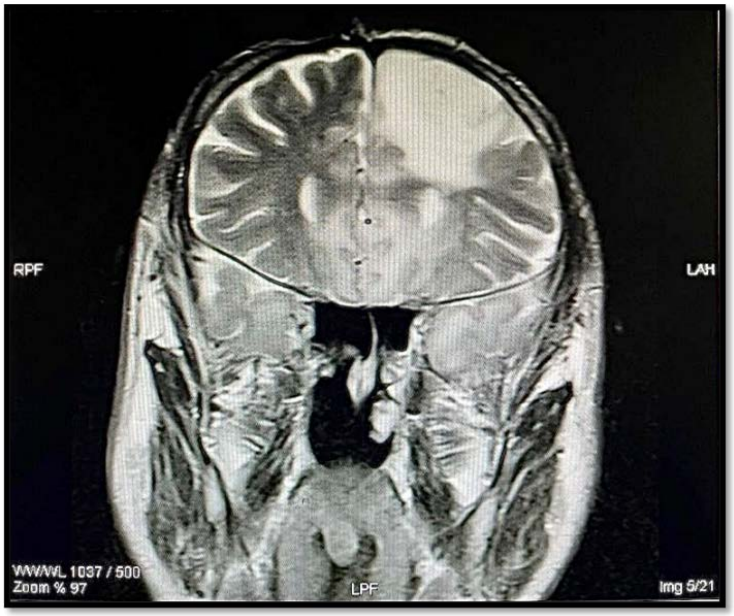
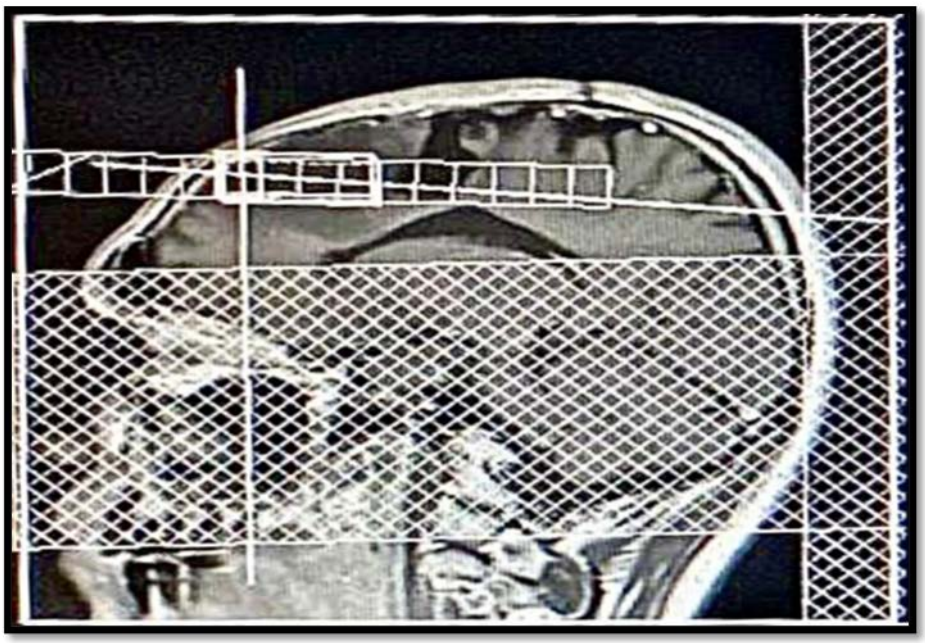
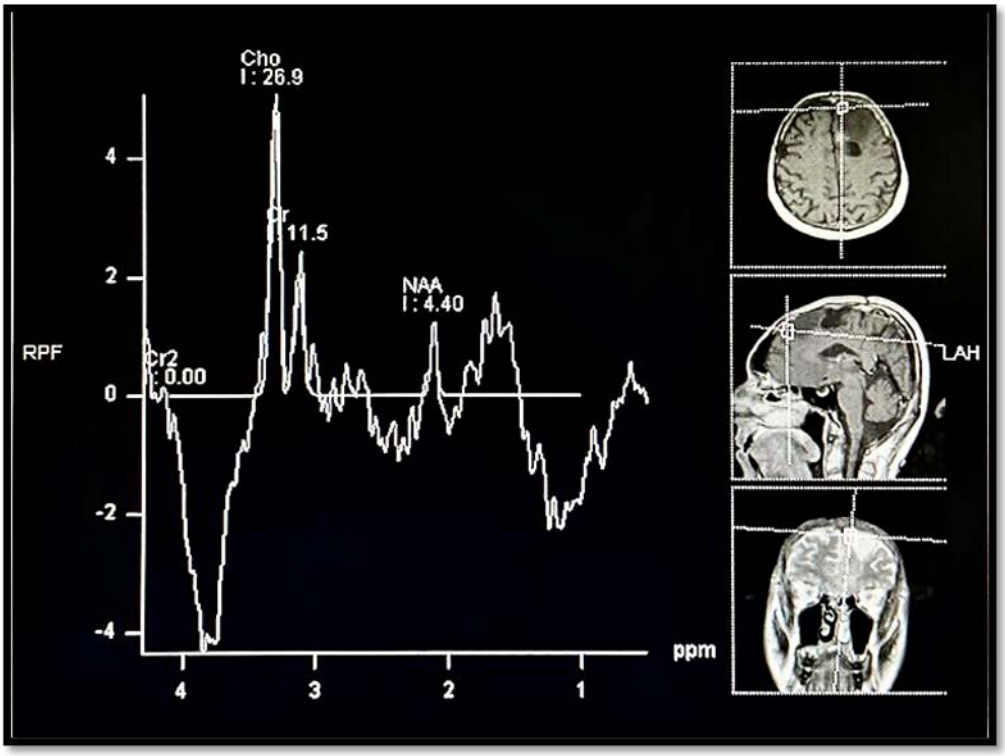
FIGURES



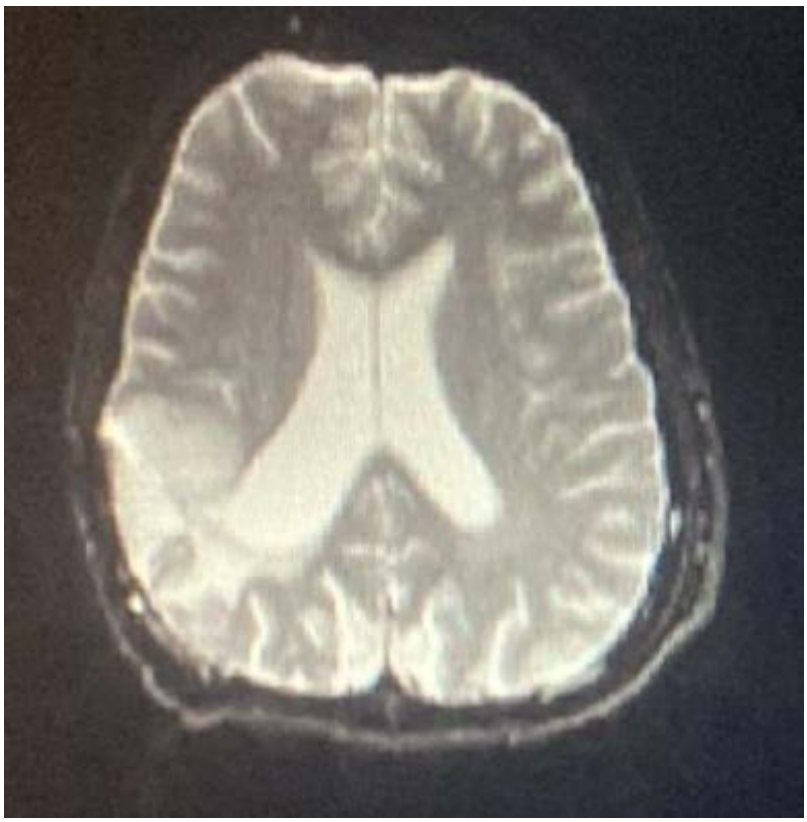
Case 1 Figure 1: Coronal plane demonstrates a high T2 signal.



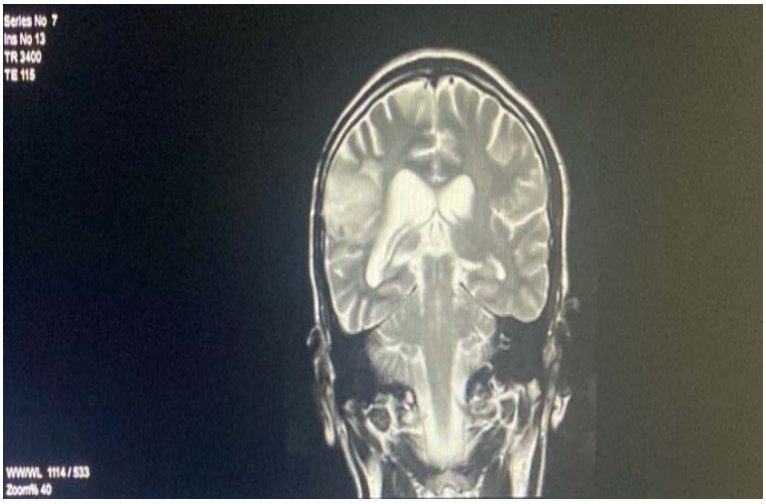
Case 1 Figure 2: MRS single voxel sagittal plan



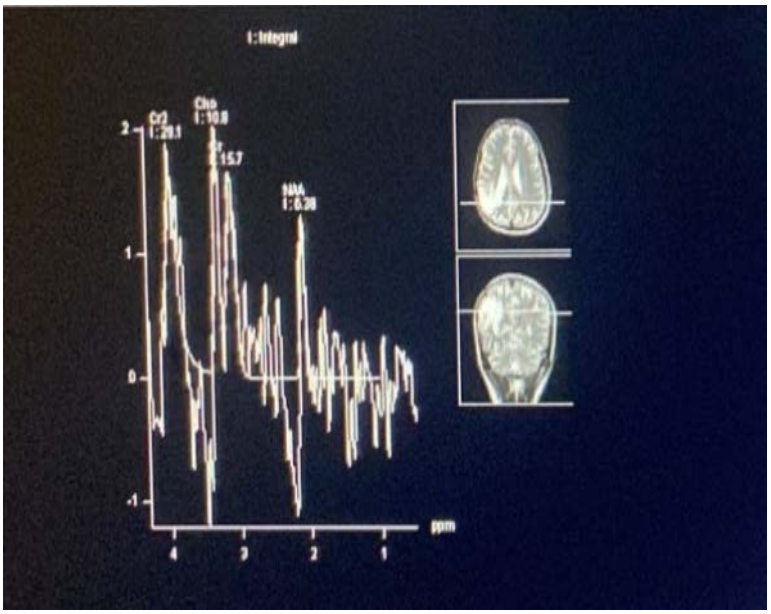
Case 1 Figure 3: shows the location of the Lesion and the MRS plan, and the result of the chemical shift.



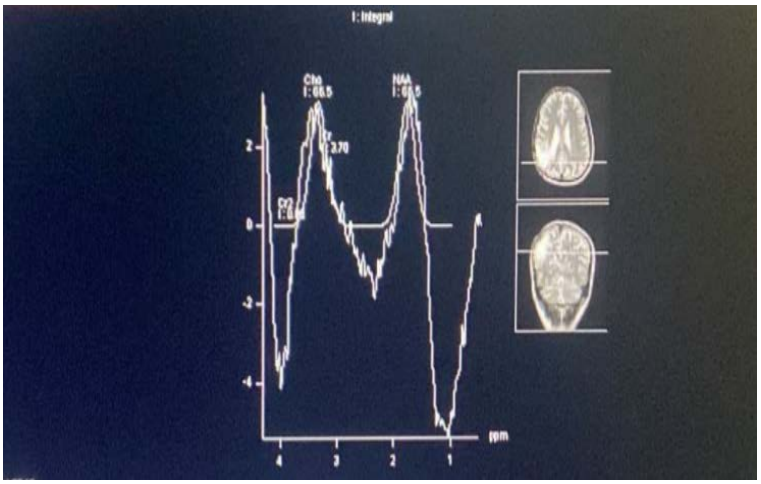
Case 2 Figure 1: Axial T2 brain MRI demonstrating a right parieto-occipital diffuse astrocytoma



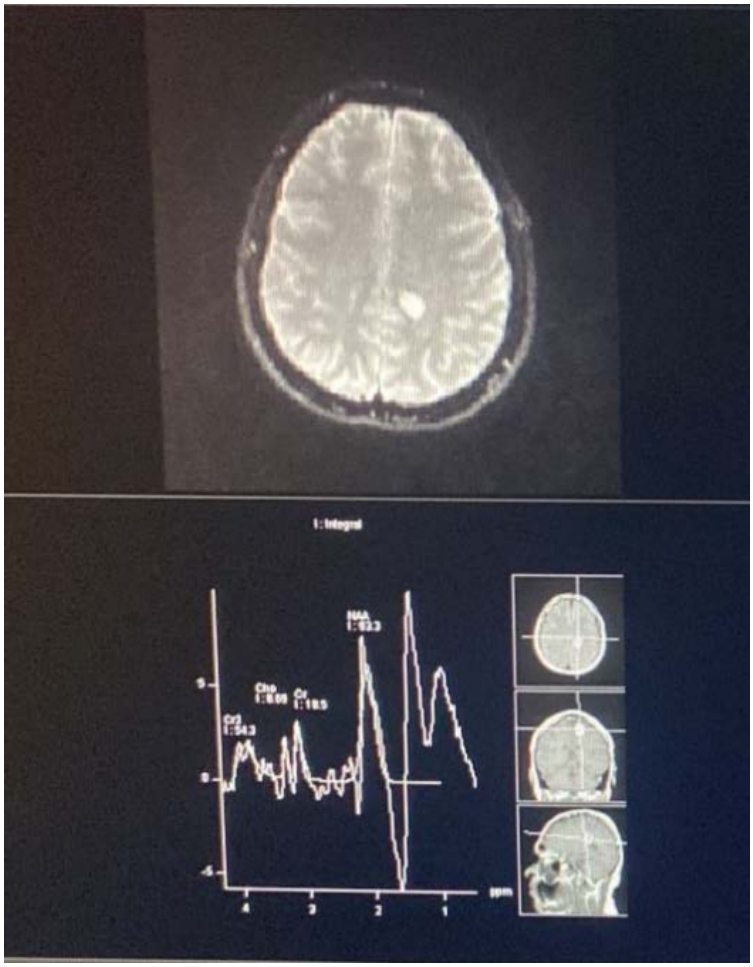
Case 2 Figure 2: Coronal T2 brain MRI demonstrating a right parieto-occipital diffuse astrocytoma



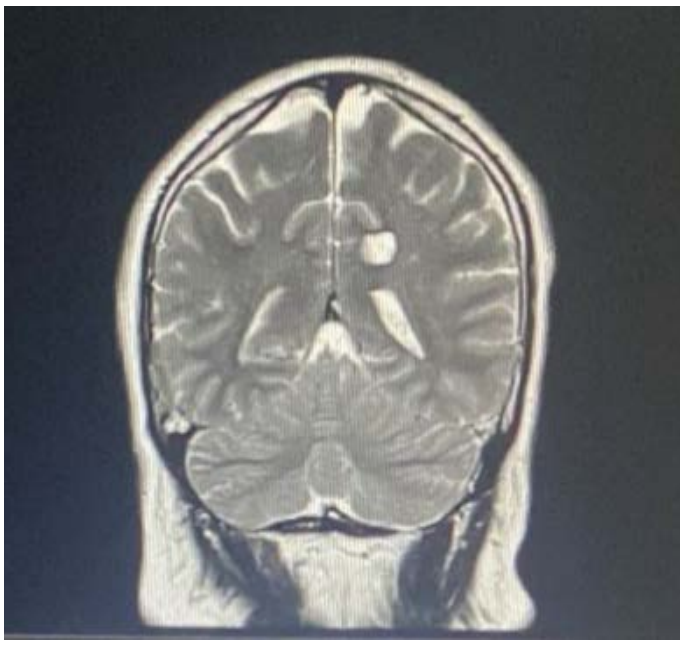
Case 2 Figure 3: Spectroscopic analysis shows a reversed NAA/choline curve.



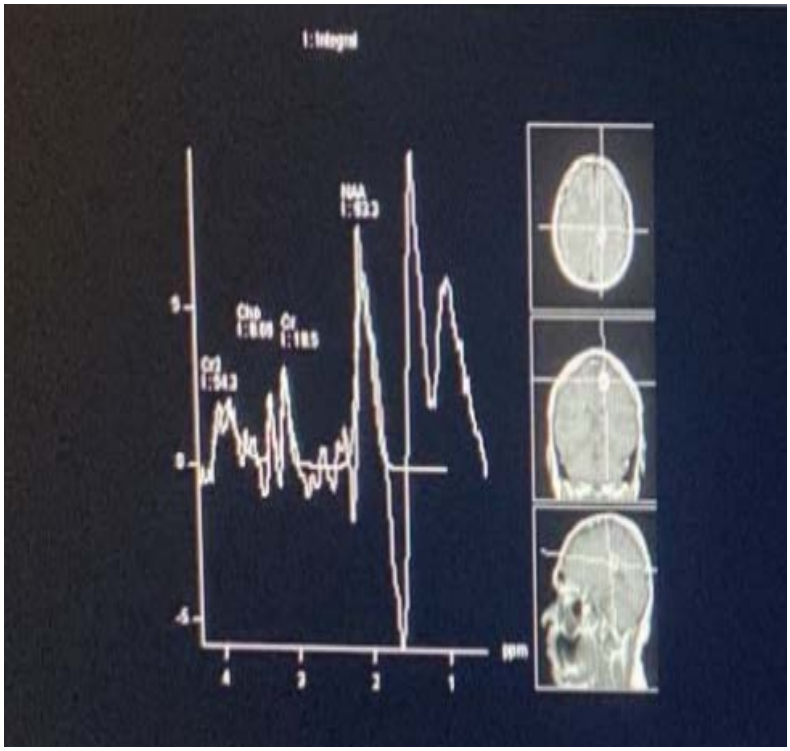
Case 2 Figure 4: Spectroscopic analysis show NAA/choline peaks curve



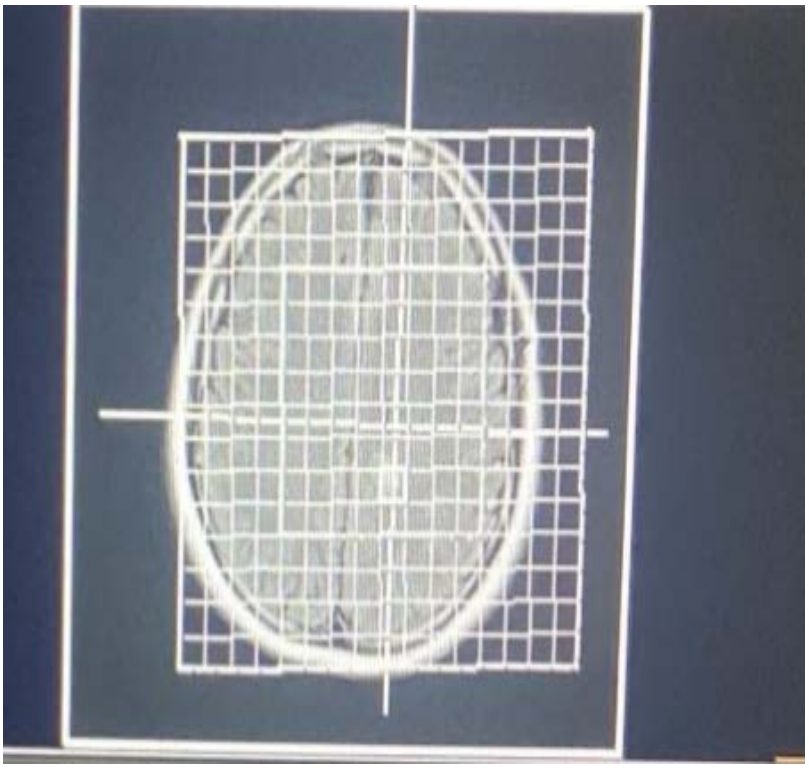
Case 3 Figure 1: Axial FLAIR MRI showing a lesion in the left posterior parietal region and spectroscopic analysis using a single voxel.



Case 3 Figure 2: Coronal T2 brain MRI show the lesion



Case 3 Figure 3: A single voxel showed a low choline and creatinine ratio in spectroscopic analysis.



Case 3 Figure 4: Axial MRI show multivoxel analysis.

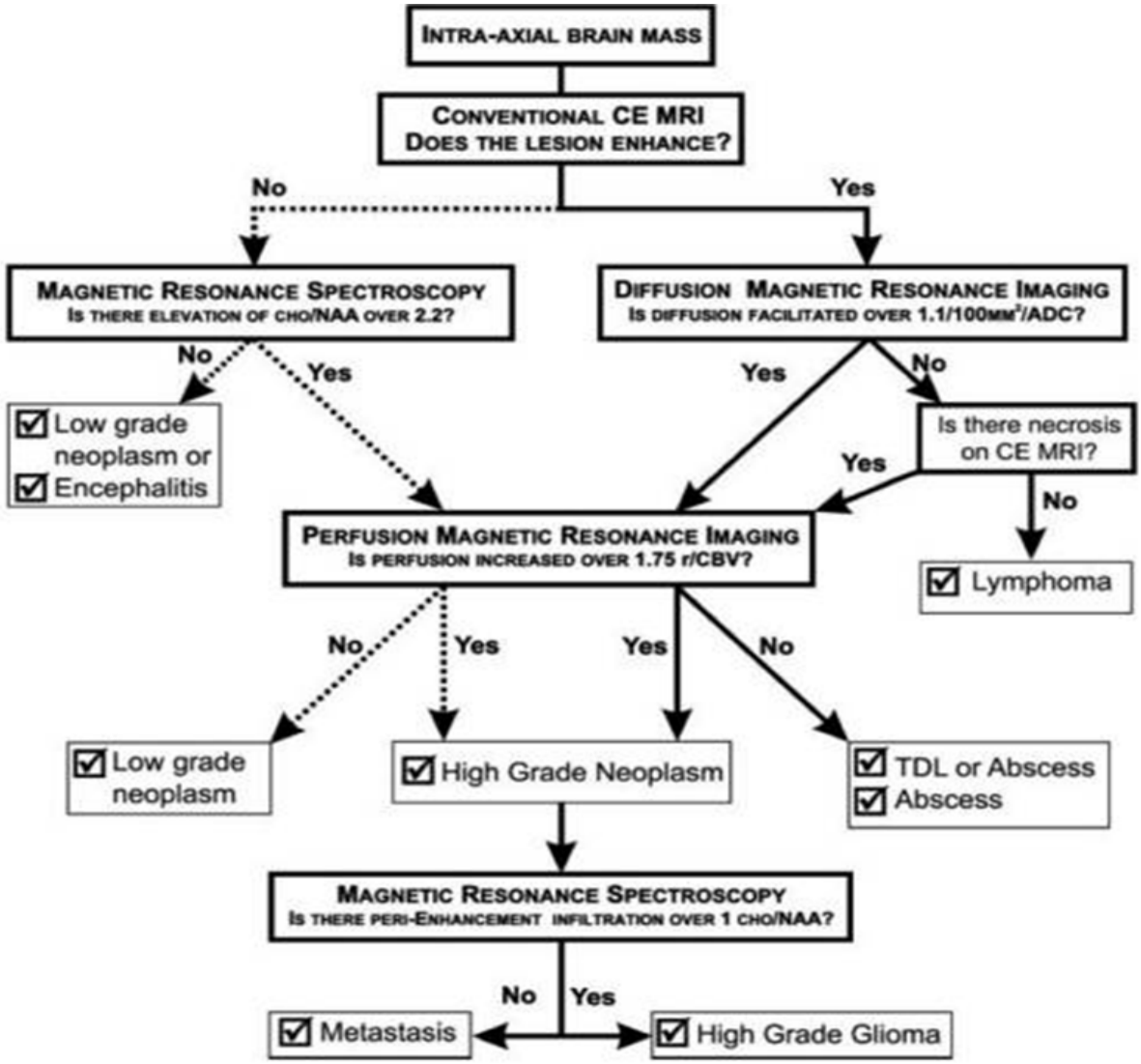


Chart 1: Flowchart for determining the brain lesion type based on conventional contrast-enhanced MRI, diffusion-weighted MRI, MR spectroscopy, and MR perfusion imaging.
1.1/100MM2/ADC = 1.1×10−3 mm2/sec, ADC = Apparent Diffusion Coefficient, CE = Contrast Material Enhanced, Cho = Choline, NAA = N-Acetylaspartate, rCBV = Relative Cerebral Blood Volume, TDL = Tumefactive Demyelinating Lesion. Reproduced with permission from equation [11].

KEYWORDS

Intracranial, Brain lesion, MRI Spectroscopy, Space-occupying lesion, Astrocytoma

ABBREVIATIONS

MRS = Magnetic Resonance Spectroscopy
MRI = Magnetic Resonance Imaging
SOL = Space-Occupying Lesion
Cho/Cr = Choline/Creatine
Cho/NAA = Choline/N-Acetyl Aspartate
Lac = Lactate, Lac/Cr
Glc = Glucose
Gln = Glutamine
CH2-Lip = CH2 Lipids
Tau = Taurine
Cit = Citrate
Ala = Alanine
ADC = Apparent Diffusion Coefficient
CE = Contrast Material Enhanced
Cho = Choline
NAA0 =N-Acetylaspartate
Rcbv = Relative Cerebral Blood Volume
TDL = Tumefactive Demyelinating Lesion
WHO = World Health Organization
OS = Overall Survival

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